EXHIBIT O

H

Impax Laboratories, Inc. v. Aventis Pharmaceuticals Inc.
D.Del.,2007.

United States District Court,D. Delaware.
IMPAX LABORATORIES, INC., Plaintiff and Counterdefendant,
v.
AVENTIS PHARMACEUTICALS INC., Defendant and Counterclaimant.
Civil Action No. 02-581-JJF.

July 19, 2007.

Background: Pharmaceutical company brought action against patent holder seeking declaratory judgment that it did not infringe, induce infringement of, or contribute to infringement of patent for use of antiglutamate drug to treat amyotrophic lateral sclerosis (ALS) by filing Abbreviated New Drug Application (ANDA). The United States District Court for the District of Delaware, Farnan, J., 235 F.Supp.2d 390 and 333 F.Supp.2d 265, granted judgment for patent holder. Plaintiff appealed. The Court of Appeals, 468 F.3d 1366, affirmed in part, vacated in part, and remanded. On remand, the Court took up remanded issues.

Holdings: The District Court, Farnan, J., held that:

(1) patent which disclosed pharmaceutical compounds useful for treatment of medical conditions associated with effects of glutamate that it defined as compounds of particular formula did not enable person of ordinary skill in art to treat amyotrophic lateral sclerosis (ALS) with chemical compound riluzole, and

(2) patent that was not enabled could not anticipate patent on riluzole.

Ordered accordingly.

West Headnotes

[1] Patents 291 65

291 Patents
291II Patentability
291II(D) Anticipation
291k63 Prior Patents
291k65 k. Sufficiency of Description. Most Cited Cases

In the patent context, a claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.

[2] Patents 291  99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases

In the patent context, an enabled prior art reference must teach a person of ordinary skill in the art to make or carry out the claimed invention without undue experimentation.

[3] Patents 291  99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases

Factors relevant in determining whether undue experimentation is required, so as to undermine enabling requirement for a patent, include: (1) the quantity of experimentation; (2) the amount of direction or guidance present; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

[4] Patents 291  99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases

Undue experimentation that undermines the enabling requirement for a patent is evaluated from the vantage point of those experienced in the field of the invention; test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in

© 2008 Thomson/West. No Claim to Orig. U.S. Govt. Works.

which the experimentation should proceed.

[5] Patents 291 ⚿99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases
Patent, which disclosed pharmaceutical compounds useful for treatment of medical conditions associated with effects of glutamate that it defined as compounds of particular formula, did not enable person of ordinary skill in art to treat amyotrophic lateral sclerosis (ALS) with chemical compound riluzole, and thus patent was invalid for lack of enablement, since link between riluzole and treatment of ALS was speculative and undue experimentation would have been required to establish such link; although patent specifically named riluzole, it did so to exclude it from claimed invention or to identify it as "raw" or starting material for synthesis of other compounds.

[6] Patents 291 ⚿65

291 Patents
291II Patentability
291II(D) Anticipation
291k63 Prior Patents
291k65 k. Sufficiency of Description. Most Cited Cases
Patent that was not enabled could not anticipate other patent.

Patents 291 ⚿328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original Utility. Most Cited Cases
5,236,940. Invalid.

Patents 291 ⚿328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original Utility. Most Cited Cases
5,527,814. Valid.

*430 Philip J. McCabe, Esquire of Kenyon & Kenyon LLP, San Jose, CA, C. Kyle Musgrove, Esquire; Michael M. Shen, Esquire and Aimee N. Soucie, Esquire of Kenyon & Kenyon LLP, Washington, D.C., Mary B. Matterer, Esquire of Morris James LLP, Wilmington, DE, Attorneys for Plaintiff and Counterdefendant, Impax Laboratories, Inc.
Joseph P. Kirk, Esquire of Aventis Pharmaceuticals Inc., Bridgewater, NJ, Paul H. Berghoff, Esquire; Curt J. Whitenack, Esquire; James C. Gumina, Esquire; Jeremy E. Noe, Esquire and Paul S. Tully, Esquire of McDonnell Boehnen Hulbert & Berghoff, Chicago, IL, Jeffrey B. Bove, Esquire of Connolly Bove Lodge & Hutz, Wilmington, DE, Attorneys for Defendant and Counterclaimant, Aventis Pharmaceuticals Inc.

MEMORANDUM OPINION

FARNAN, District Judge.
This action was remanded by the Court of Appeals for the Federal Circuit for a determination of whether U.S. Patent No. 5,236,940 (the " 940 patent") is enabled, and if so, whether U.S. Patent Mo. 5,527,814 (the " 814 patent") is invalid as anticipated. The Court requested, and the parties filed, supplemental briefing on the remanded issues. For the reasons discussed, the Court concludes that the 940 patent is not enabled, and therefore, does not invalidate the 814 patent on the grounds of anticipation.

I. BACKGROUND

Plaintiff and Counterclaim Defendant, Impax Pharmaceuticals, Inc. ("Impax"), filed this action against Defendant and Counterclaimant, Aventis Pharmaceuticals Inc. ("Aventis"), seeking a declaratory judgment of noninfringement and invalidity of the 814 patent. In response, Aventis filed a motion for a preliminary injunction, which the Court granted on December 12, 2002. Since that time, Impax has been enjoined from marketing generic riluzole tablets for the treatment of patients with amyotrophic lateral sclerosis ("ALS").

On summary judgment, the Court concluded that Impax would infringe and induce infringement of claims 2 and 3 of the 814 patent. A bench trial was held on the remaining issues of: (1) whether the 814 patent was invalid as anticipated by either the 940 patent or French Patent Application No. 2,264,624 (the " 624 application") and (2) whether the 814

© 2008 Thomson/West. No Claim to Orig. U.S. Govt. Works.

patent was unenforceable due to inequitable conduct. The Court concluded that Impax failed to establish either anticipation or unenforceability, and the Court declined to revisit the questions of infringement adjudicated on summary judgment. Impax appealed the Court's decision.

On appeal, the Federal Circuit affirmed the Court's decision on the issues of inequitable conduct and anticipation in light of the 624 application. *Impax Laboratories, Inc. v. Aventis Pharmaceuticals Inc. ("Impax II")*, 468 F.3d 1366 (Fed.Cir.2006). However, the Federal Circuit vacated the Court's decision regarding anticipation in light of the 940 patent. Specifically, the Federal Circuit concluded that the Court erred in concluding that the 940 patent was not an enabling prior art reference because there was no evidence that the 940 patent was effective. The Federal Circuit noted that under *Rasmusson v. SmithKline Beecham*, 413 F.3d 1318 (Fed.Cir.2005), "a section 102 prior art reference does not have to be 'effective' to be enabling and thus anticipating." *Impax II*, 468 at 1383. Accordingly, the Federal *431 Circuit remanded the case for the Court to determine whether the disclosure of formula I in the 940 patent enables a person of ordinary skill in the art to carry out the invention claimed in claims 1-5 of the 814 patent. Stated another way, the Court must determine "whether the 940 patent enables a person of ordinary skill in the art to treat ALS with riluzole," without regard to the efficacy of such treatment. *Id.* at 1384. If the 940 patent is enabled, the Court must then determine whether it anticipates claims 1-5 of the 814 patent. If it is not enabled, the Court must then conclude that claims 1-5 of the 814 patent are not anticipated by the 940 patent. *Id.*

II. THE PARTIES' CONTENTIONS

By its supplemental brief, Aventis contends that the Court has already made the necessary findings to conclude that the 940 patent is not enabled and does not anticipate the claims of the 814 patent. Aventis contends that these findings were not disturbed by the Federal Circuit on appeal and points out that in his concurring opinion, Judge Rader wrote:

> the district court has found that the disclosure does not make even a suggestion of disclosure to one of skill in the art. Beyond the efficacy question, the 940 patent does not even disclose the necessary suggestion to enable one of ordinary skill in the art to look to riluzole for the treatment of ALS in the first place. Thus, I would affirm the district court's determination of [no] anticipation without requiring a remand.

(D.I. 255 at 6) (quoting *Impax II*, 468 F.3d at 1384) (Rader, J., concurring in part). Aventis also contends that the Federal Circuit's determination that the 624 application does not anticipate the 814 supports a conclusion that the 940 patent does not anticipate the 814 patent. In this regard, Aventis points out that the specification of the 940 patent is virtually identical to the 624 application with the exception of a proviso in the 940 patent*excluding* riluzole from the invention. Aventis contends that the exclusion of riluzole cannot be sufficient to lead one skilled in the art to recognize that riluzole can be used to treat ALS. Like the 624 application, Aventis contends that the 940 patent: (1) discloses hundreds or thousands of formula I compounds and numerous diseases, yielding thousands of possible combinations, (2) provides no direction or guidance to arrive at the claimed combination of using riluzole to treat ALS, and (3) does not disclose any working examples of the claimed combination. Thus, Aventis contends that the 940 patent is not enabled, and therefore, it cannot invalidate the 814 patent as anticipated.

In the alternative, Aventis contends that even if the 940 patent is enabled, it does not anticipate the 814 patent because the subject matter of the 814 patent does not exist in the 940 patent. Aventis contends that the same deficiencies which prevent the 940 patent from being enabled also prevent the 940 patent from clearly and convincingly anticipating the 814 patent.

In response, Impax contends that the Federal Circuit recognized that the 940 patent "includes riluzole as a formula I compound, suggests that formula I compounds may be used to treat ALS, and provides some dosage information." (D.I. 262 at 3) (quoting *Impax II*, 468 F.3d at 1383). Impax contends that this information is sufficient to support a finding that the 940 patent is enabled. Impax maintains that the 940 patent is different from the 624 application because it specifically names riluzole as a formula I compound. Thus, Impax contends that the specification of the 940 patent is sufficient to be enabled.

Impax further contends that anticipation only requires an enabled prior art reference. Thus, Impax contends that if the *432 940 patent is enabled, it anticipates the 814 patent.

© 2008 Thomson/West. No Claim to Orig. U.S. Govt. Works.

III. DISCUSSION

[1][2] "A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354, 65 USPQ2d 1385, 1416 (Fed.Cir.2003). The disclosure in an enabling reference must be sufficient to put one skilled in the art in possession of the invention. *In re Donohue*, 766 F.2d 531, 533 (Fed.Cir.1985). Stated another way, an enabled prior art reference must teach a person of ordinary skill in the art to make or carry out the claimed invention without undue experimentation. *Minnesota Mining and Manufacturing Co. v. Chemque, Inc.*, 303 F.3d 1294, 1301 (Fed.Cir.2002).

[3][4] Undue experimentation is evaluated from the vantage point of those experienced in the field of the invention. "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed...."*In re Wands*, 858 F.2d 731, 737 (Fed.Cir.1988). Factors relevant in determining whether undue experimentation is required include: (1) the quantity of experimentation; (2) the amount of direction or guidance present; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. *Id.*

[5] Evaluating the 940 patent in light of these legal principles, the Court concludes that the 940 patent is not enabled. Like the 624 application, the 940 patent embraces in formula I hundreds to thousands of different compounds and cites numerous medical conditions associated with the effects of glutamate. Nothing in the 940 patent directs one skilled in the art to recognize that riluzole can be used to treat ALS. Although the 940 patent specifically names riluzole, it does so to exclude it from the claimed invention or to identify it as a "raw" or starting material for the synthesis of other compounds. In these circumstances, the Court is not persuaded that the mere mention of riluzole is sufficient to put one skilled in the art in the possession of the claimed invention as is required to support a conclusion of enablement.

The Court further finds that undue experimentation would be required to link riluzole with the treatment of ALS. Impax directs the Court to dosage information contained in the 940 patent to suggest that undue experimentation would not be required; however, that dosage information amplifies the preceding paragraph of the 940 patent which states:

> In human therapy, *the compounds according to the invention* are especially useful in the treatment and prevention of convulsive phenomena, schizophrenic disorders, and in particular the deficiency forms of schizophrenia, sleep disorders, phenomena linked to cerebral ischaemia and also neurological conditions in which glutamate may be implicated, such as Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis and olivopontocerebellar atrophy.

940 patent, col. 13, ll. 33-42 (emphasis added).

[6] As the Court has recognized, the invention specifically excludes riluzole, and therefore, the Court cannot conclude that the dosage information which pertains to the compounds of the invention, would be helpful in placing one skilled in the art in possession of the claimed invention. ***433** Moreover, the dosage guidelines are broad and not specific to any of the hundreds of formula I compounds of the claimed invention or to any of the listed diseases. As the above passage indicates, the compounds of the claimed invention are associated with the treatment of at least 8 different diseases, and there is nothing in the 940 patent which would lead one to recognize that any specific compound, let alone riluzole, would be used to treat any specific disease, let alone ALS.[FN1]The 940 patent also identifies four preferred compounds, but riluzole is not one of them, and there are no working examples in the patent for the treatment of ALS with riluzole. Because the link between riluzole and the treatment of ALS is speculative and undue experimentation would be required to establish such a link, the Court cannot conclude that the 940 patent is enabled. Having concluded that the 940 patent is not enabled, the Court further concludes that it cannot anticipate the 814 patent.

FN1. The Court's observation applies with equal force to the passage identified by the Federal Circuit and cited by Impax discussing not just the compounds of the invention, but the compounds of formula I, in connection with the treatment of certain

© 2008 Thomson/West. No Claim to Orig. U.S. Govt. Works.

> diseases. This passage states:
> The compounds of formula (1) and their salts possess advantageous pharmacological properties. These compounds are useful in the treatment of medical conditions associated with the effects of glutamate in which it is desirable to inhibit such effects at least partially. They are active with respect to glutamate-induced convulsions and are hence useful in the treatment and prevention of convulsive phenomena, schizophrenic disorders, and in particular the deficiency forms of schizophrenia, sleep disorders, phenomena linked to cerebral ischaemia and also neurological conditions in which glutamate may be implicated, such as Alzheimer's disease, Huntington's chorea, [ALS] and olivopontocerebellar atrophy.
> 940 patent, col. 2, l. 63-col. 3, l. 8. While riluzole is not part of the claimed invention it is a formula I compound. However, there is nothing in the quoted passage which would identify riluzole from the multitude of formula I compounds and single out ALS as one of the at least 8 diseases mentioned. Accordingly, this passage does not undercut the Court's conclusion that the 940 patent is neither enabled, nor anticipated.

IV. CONCLUSION

For the reasons discussed, the Court concludes that the 940 patent is not enabled, and therefore, does not anticipate the 814 patent. Accordingly, the Court will enter judgment in favor of Aventis and against Impax.

An appropriate Order accompanying this Memorandum Opinion and a Final Judgment Order will be entered.

ORDER

At Wilmington, this 19 day of July 2007, for the reasons set forth in the Memorandum Opinion issued this date;

IT IS HEREBY ORDERED that:

1. U.S. Patent No. 5,236,940 is not enabled, and therefore, does not anticipate U.S. Patent No. 5,527,814.

2. U.S. Patent No. 5,527,814 is not invalid as anticipated.

D.Del.,2007.
Impax Laboratories, Inc. v. Aventis Pharmaceuticals Inc.
496 F.Supp.2d 428

END OF DOCUMENT

© 2008 Thomson/West. No Claim to Orig. U.S. Govt. Works.